

## REMARKS

Claims 1, 5, 19-20, 22-43, 55, 58-59 and 66-71 were pending in the present application. Claims 23-24, 26-29, 32-43, 66-69 and 71 were withdrawn from consideration. With this amendment, Applicants have canceled claims 1, 5, 19-20, 22-40, 42-43, 55, 58, 66-67 and 70-71 without prejudice.<sup>1</sup> Applicants have also added new claims 72-78.

These amendments are made without prejudice. Applicants reserve the right to prosecute the deleted or canceled subject matter in related applications. No new matter is added by these amendments.

Support for new claim 72 may be found *inter alia* on page 5, line 9 to page 6, line 20; on page 12, lines 4-6 and 27-28, on page 15, lines 20-24; on page 16, lines 10 and 16-19; on page 18, lines 1-32; on page 45, lines 6-9; and on page 49, lines 18-20 of the specification.

Support for new claim 73 may be found *inter alia* on page 5, line 9 to page 6, line 26; on page 12, lines 4-6 and 27-28, on page 15, lines 20-24; on page 16, lines 10 and 16-19; on page 18, lines 1-32; on page 45, lines 6-9; and on page 49, lines 18-20 of the specification.

Support for new claim 74 may be found *inter alia* on page 5, line 9 to page 6, line 20; on page 15, lines 20-24; on page 16, lines 10 and 16-19; on page 18, lines 1-32; on page 41, lines 11-22, and on page 45, lines 6-9 of the specification.

Support for new claim 75 may be found *inter alia* on page 5, line 9 to page 6, line 26; on page 15, lines 20-24; on page 16, lines 10 and 16-19; on page 18, lines 1-32; on page 41, lines 11-22, and on page 45, lines 6-9 of the specification.

Support for new claim 76 may be found *inter alia* on page 5, line 9 to page 6, line 20; on page 15, lines 20-24; on page 16, lines 10 and 16-19; on page 12, lines 4-6 and 27-28, on page 18, lines 1-32; on page 41, lines 11-22, on page 45, lines 6-9; and on page 49, lines 18-20 of the specification.

Support for new claim 77 may be found *inter alia* on page 5, line 9 to page 6, line 26; on page 15, lines 20-24; on page 16, lines 10 and 16-19; on page 12, lines 4-6 and 27-28, on page 18, lines 1-32; on page 41, lines 11-22, on page 45, lines 6-9; and on page 49, lines 18-20 of the specification.

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<sup>1</sup> Applicants note that in the Office Action dated October 5, 2007, the Examiner has not addressed the status of claim 55. However, in view of the cancellation of claim 55, the omission is moot.

Support for new claim 78 may be found *inter alia* on page 41, line 13 of the specification.

After entry of these amendments, claims 68-69 and 72-78 will be pending.

Entry of the foregoing amendments and consideration of these remarks are respectfully requested.

***Interview Summary Record***

Applicants and Applicants' representatives thank Examiner Marcela Cordero Garcia and Supervisory Patent Examiner ("SPE") Cecilia J. Tsang, for the courtesy of the telephonic interview dated February 6, 2008 in connection with the above-identified application (the "Interview"), between Examiner Marcela Cordero Garcia and SPE Cecilia J. Tsang, and the Applicants' representatives, Adriane M. Antler and David J. Kerwick. Pursuant to 37 C.F.R. § 1.133 and M.P.E.P. 713.04, Applicants present this Interview Summary Record of the Interview.

Ms. Antler addressed the pending rejection of claims 1, 5, 19-20, 22-25, 30-31, 58-59 and claim 70 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 6,001,965 ("the '965 patent") in view of International Publication No. WO 02/057786 ("the '786 application") and Greene, et al., Protective Groups in Organic Synthesis, 1999 ("Greene"). Ms. Antler directed the Examiners' attention to the Declaration of Dr. Andrew P. Mazar Under 37 C.F.R. § 1.132 ("Dr. Mazar's Declaration") which was filed May 15, 2007. In particular, Ms. Antler noted that two compounds, Ac-PHSC(Me)N-NH<sub>2</sub>, and Ac-PHSC(acetyl)N-NH<sub>2</sub>, respectively claimed in pending claims 68 and 69, were unexpectedly more active at inhibiting tumor growth than the parent PHSCN compound disclosed in the '965 patent and the '786 application. Therefore, Ms. Antler suggested that amending the claims to limit them to these two compounds should overcome the obviousness rejection. Examiner Cordero Garcia and SPE Tsang both agreed that such an amendment would overcome the obviousness rejection. Ms. Antler asked if a claim to a pharmaceutical composition comprising the above two compounds would also be allowable. Examiners Cordero Garcia and Tsang both acknowledged that it would.

Ms. Antler next asked if Applicants could also add method of treatment claims involving use of the two aforementioned compounds. Examiner Cordero Garcia and SPE

Tsang stated that adding claims to methods of treating lung cancer using such compounds would be allowable.

### ***Claim Rejections - 35 U.S.C. § 103***

On pages 3-6 of the October 5, 2007 Office Action, the Examiner maintained the rejection of claims 1, 5, 19-20, 22-25, 30-31, 58-59 and claim 70 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 6,001,965 (“the ‘965 patent”) in view of International Publication No. WO 02/057786 (“the ‘786 application”) and Greene, et al., *Protective Groups in Organic Synthesis*, 1999 (“Greene”).

The Examiner alleged that from the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention and therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

In response, Applicants have canceled claims 1-67 and 70-71. Applicants have also added new claims 72-78 such that the currently pending claims are 68-69 and 72-78.

Claim 68 is directed to the compound Ac-PHSC(Me)N-NH<sub>2</sub>, and claim 69 is directed to the compound Ac-PHSC(acetyl)N-NH<sub>2</sub>. The compounds of claims 68 and 69 exhibit unexpected results, which are objective evidence of nonobviousness.

The factual determinations relevant to the obviousness inquiry include: (1) the scope and content of the prior art; (2) the differences between the claimed invention and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations, if any, such as commercial success, unexpected results, copying, long-felt but unresolved need, and the failure of others to develop the invention. *Graham v. John Deere Co.*, 383 U.S. 1, 17, 86 S.Ct. 684, 15 L.Ed.2d 545, 148 USPQ 459, 467 (1966).

*Syntex (U.S.A.) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1378 (Fed. Cir. 2005). The unexpected results exhibited by the compounds of the claimed invention are described in the Declaration of Dr. Andrew P. Mazar Under 37 C.F.R. § 1.132 (“Dr. Mazar’s Declaration”) which was filed May 15, 2007.

Dr. Mazar’s Declaration describes the biological activities (inhibition of tumor growth) of numerous peptides described in the subject application. The most active compound, Ac-PHSC(Me)N-NH<sub>2</sub>, which has a side chain of CH<sub>2</sub>SCH<sub>3</sub> on the 4<sup>th</sup> amino acid, unexpectedly

inhibited tumor growth greater than 3 times better than Ac-PHSCN-NH<sub>2</sub> (SEQ 86 of the '965 patent), which has a side chain of CH<sub>2</sub>SH (see paragraph 6, Table 1 of Dr. Mazar's Declaration). Claim 68 is directed to the compound Ac-PHSC(Me)N-NH<sub>2</sub>. The other compound with an unexpectedly high degree of activity is the S-acetyl compound (Ac-PHSC(acetyl)N-NH<sub>2</sub>) which was almost as active as the Ac-PHSC(Me)N-NH<sub>2</sub> compound and inhibited tumor growth over 2 times better than Ac-PHSCN-NH<sub>2</sub>. Claim 69 is directed to the compound Ac-PHSC(acetyl)N-NH<sub>2</sub>. The inhibition of tumor growth by Ac-PHSC(Me)N-NH<sub>2</sub> and Ac-PHSC(acetyl)N-NH<sub>2</sub> were both unexpected (see paragraph 7 of Dr. Mazar's Declaration). One skilled in the art would have no expectation from the combined teaching of the '965 patent, the '786 application and Greene that an improvement of 2-3 x in the inhibition of tumor growth could be achieved with the substitution of SH by SCH<sub>3</sub> or S-acetyl.

Furthermore, Dr. Mazar states in his declaration that the data provided in Dr. Mazar's Declaration show the lack of predictability around the substitution pattern of the side chain of the 4<sup>th</sup> amino acid of the pentapeptides (see paragraph 7 of Dr. Mazar's Declaration). As described by Dr. Mazar, other alkyl substitutions on the S of the side chain of the 4<sup>th</sup> amino acid produced pentapeptides which were much less capable than Ac-PHSC(Me)N-NH<sub>2</sub> or Ac-PHSCN-NH<sub>2</sub>, (SEQ 86) at inhibiting the growth of tumors. For example, the S-t-butyl compound (Ac-PHSC(t-Butyl)N-NH<sub>2</sub>) and the S-(CH<sub>2</sub>)OCH<sub>3</sub> compound (Ac-PHSC(2-methoxyethyl)N-NH<sub>2</sub>) are much less active than either the Ac-PHSC(Me)N-NH<sub>2</sub> or Ac-PHSCN-NH<sub>2</sub> compounds. Moreover, other acyl substituted compounds are also much less capable of inhibiting tumor growth. The S-pivoyl compound (Ac-PHSC(pivoyl)N-NH<sub>2</sub>) had approximately the same activity as Ac-PHSCN-NH<sub>2</sub> and was much less active than Ac-PHSC(acetyl)N-NH<sub>2</sub>, while the S-cyclohexanoyl (Ac-PHSC(cyclohexanoyl)N-NH<sub>2</sub>), S-benzoyl (Ac-PHSC(benzoyl)N-NH<sub>2</sub>) and S-alloc (Ac-PHSC(alloc)N-NH<sub>2</sub>) compounds were all much less active than either Ac-PHSCN-NH<sub>2</sub> or Ac-PHSC(acetyl)N-NH<sub>2</sub> (see paragraph 7 of Dr. Mazar's Declaration).

The unexpected results for the compounds in claims 68 and 69 demonstrate the nonobviousness of these compounds. Thus, claims 68 and 69 are nonobvious.

The compounds described above were tested in an in vivo assay for inhibition of tumor growth using lung carcinoma cells (see paragraph 5 of Dr. Mazar's Declaration). New claims 74-77 are directed to a method of treating lung cancer. As discussed in the interview

summary above, these claims should be deemed allowable. Claims 72 and 73, directed to pharmaceutical compositions, also should be deemed allowable.

For the above reasons, Applicants respectfully request the Examiner find that claims 68-69 and 72-78 would not be obvious to one skilled in the art over the '965 patent in view of the '786 application and Greene.

***Double Patenting***

The Examiner has provisionally rejected claims 1, 5, 19-20, 22-25, 30-31 and 58-59 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 64-65 of co-pending Application No. 10/722,843 ("the '843 application").

Applicants note that the '843 application has been abandoned, thus obviating the rejection. A copy of the Notice of Abandonment issued December 28, 2007 by the U.S. Patent and Trademark Office in connection with U.S. Application No. 10/722,843 is attached as Exhibit A.

For the above reason, Applicants respectfully request withdrawal of the double patenting rejection.

**CONCLUSION**

Applicants respectfully request that the present amendments and remarks be entered and made of record in the instant application. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested. If any issues remain in connection herewith, the Examiner is invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: March 5, 2008

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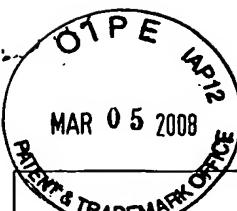
Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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### Notice of Abandonment

#### Application No.

10/722,843

#### Applicant(s)

TERNANSKY ET AL.

#### Examiner

Art Unit

Marcela M. Cordero Garcia

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

This application is abandoned in view of:

1.  Applicant's failure to timely file a proper reply to the Office letter mailed on 13 June 2007.
  - (a)  A reply was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply (including a total extension of time of \_\_\_\_\_ month(s)) which expired on \_\_\_\_\_.
  - (b)  A proposed reply was received on \_\_\_\_\_, but it does not constitute a proper reply under 37 CFR 1.113 (a) to the final rejection. (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
  - (c)  A reply was received on \_\_\_\_\_ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
  - (d)  No reply has been received.
  
2.  Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
  - (a)  The issue fee and publication fee, if applicable, was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
  - (b)  The submitted fee of \$\_\_\_\_\_ is insufficient. A balance of \$\_\_\_\_\_ is due.  
The issue fee required by 37 CFR 1.18 is \$\_\_\_\_\_. The publication fee, if required by 37 CFR 1.18(d), is \$\_\_\_\_\_.
  - (c)  The issue fee and publication fee, if applicable, has not been received.
  
3.  Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
  - (a)  Proposed corrected drawings were received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply.
  - (b)  No corrected drawings have been received.
  
4.  The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.
  
5.  The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.
  
6.  The decision by the Board of Patent Appeals and Interference rendered on \_\_\_\_\_ and because the period for seeking court review of the decision has expired and there are no allowed claims.
  
7.  The reason(s) below:

Applicant's representative confirmed abandonment via a telephonic message on 12/17/07.

/Cecilia Tsang/  
Supervisory Patent Examiner, Art Unit 1654

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.